UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,097	09/19/2006	Ana Isabel Sanz Molinero	4559-053584	1132

28289 7590 01/24/2008

THE WEBB LAW FIRM, P.C.
700 KOPPERS BUILDING
436 SEVENTH AVENUE
PITTSBURGH, PA 15219

EXAMINER	
KUMAR, VINOD	
ART UNIT	**PAPER NUMBER**
1638	

MAIL DATE	DELIVERY MODE
01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,097	SANZ MOLINERO ET AL.	
	Examiner	Art Unit	
	Vinod Kumar	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/11/07*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *10/25/07*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, claims 22-33 in the reply filed on November 2, 2007 is acknowledged and entered.

Claims 22-33 are pending.

Claims 1-21, and 34-51 are canceled.

Claims 22-33 are examined on merits in the present Office action. This restriction is made FINAL.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

2. An initialed and dated copy of Applicant's IDS form 1449 filed on November 8, 2007 is attached to the instant Office action. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35

U.S.C. 119(a)-(d). The certified copy of Application No. EPO 03076719.8, filed June 3, 2003 has been received.

Specification

The disclosure is objected to because of the following informalities:

4. Abstract is objected for reciting "said" after "wherein" and before "plant" in line 4. The recitation "said" should be deleted. The legal phraseology often used in patent claims, such as "said" in the instant case should be avoided. See MPEP § 608.01(b).

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example, page 8, lines 14, 16; page 9, lines 13-14, 19-21; page 10, line 30; page 12, lines 15, 25; and page 14, lines 4, 16. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. For example, page 4, lines 11, 14, 26, and page 5, line 22 of the specification contain amino acid sequences which must be referred to by their sequence identifiers as required by 37 CFR 1.821.

Description of drawings do not have SEQ ID listed with the sequences. For

example, the sequences in Figure 3 must be referred to by their sequence identifiers as required by 37 CFR 1.821.

If the sequences appearing in the specification do not have sequence ID numbers assigned to them, then an amendment to the sequence listing will be required as well. There must not be any new matter submitted, therefore it is important to be careful to include only the sequences that are already disclosed in the current specification. Failure to correct the deficiency will be held a non-responsive to this Office action.

Appropriate action is requested.

Claim Objections

7. Claims 22 and 23 are objected to because of the following informalities:

Claim 22 is objected for not reciting the full-form of the recitation "NHX". It is suggested to recite the full-form of the recitation "NHX" within the parentheses.

Claim 23 is objected for having improper article at the end of line 2. It is suggested to change "a" to --the--.

Claim 23 is objected for having improper article before "NHX" in line 3. It is suggested to change "an" to --the--.

In claim 22, it is suggested to change "a nucleic acid" in line 2 to --an isolated nucleic acid-- for clarity of the language.

In claim 23, line 3, it is suggested to change "a" before "nucleic acid" to --said--.

In claim 33, it is suggested to change "obtainable" before "plants" with --obtained--.

In claim 33, it is suggested to change "which" before "plants" in line 2 to --wherein--.

Appropriate action is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 28-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "such as" in line 3, since the phrase "such as" renders the claim indefinite because it is unclear whether the limitation following the phrase is part of the claimed invention. See MPEP § 2173.05(d).

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "such as" in line 3, since the phrase "such as" renders the claim indefinite because it is unclear whether the limitation following the phrase is part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 22-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for improving plant growth characteristics in a monocotyledonous plant comprising transforming said plant with a nucleic acid encoding an NHX protein of SEQ ID NO: 2 (SEQ ID NO: 1 encodes SEQ ID NO: 2), does not reasonably provide enablement for (a) a nucleic acid encoding any NHX protein, a homologue, derivative or active fragment thereof, (b) a nucleic acid comprising a portion of SEQ ID NO: 1, and (c) a nucleotide sequence capable of hybridizing to SEQ ID NO: 1 or a portion thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Claims are broadly drawn to a method for improving plant growth characteristics, comprising increasing, in a monocotyledonous plant, expression of a nucleic acid encoding an NHX protein, wherein said plant is grown under non-salt stress condition, or wherein said nucleic acid encodes a homologue, derivative or active fragment of said NHX protein, or wherein said nucleic acid is a portion of SEQ ID NO: 1, or a sequence capable of hybridizing to SEQ ID NO: 1 or a portion thereof.

Claim 22 is directed to a nucleic acid encoding any NHX protein which would improve monocotyledonous plant growth characteristics upon increasing its expression in said plant, and wherein said plant is grown under non-salt stress conditions.

The instant specification, however, only provides guidance for how to make and use a nucleic acid (SEQ ID NO: 1) encoding rice Na+/H+ (NHX) antiporter protein of SEQ ID NO: 2, in a method of producing transgenic rice (a monocotyledonous plant) plant having improved yield and modified plant architecture. See pages 26-30, examples 1-3, table 3.

While the specification teaches a nucleic acid sequence encoding a NHX protein of SEQ ID NO: 2, it does not teach full scope of nucleic acid sequences encoding other NHX proteins that confer improved growth characteristics in a plant grown under non-salt stress conditions.

The state of art teaches that NHX proteins are Na^+/H^+ exchanger which are implicated in diverse physiological processes. See for example, Brett et al. (Am. J. Physiol. Cell Physiol., 288:C223-C239, 2005; see page C223, 1st column, lines 5-12) who teach that NHX proteins are involved in control of cell cycle and cell proliferation,

transepithelial Na^+ movement, vesicle trafficking, cell biogenesis, and/or salt tolerance. Also see Venema et al. (JBC, 278:22453-22459), who teach that a tomato NHX2 acts as a K^+/H^+ transporter rather than Na^+/H^+ transporter, and affects accumulation of K^+ and not Na^+ in intracellular compartments. (See abstract; page 22453, last paragraph of introduction; page 22457, figure 5).

Thus one of skilled in the art would not expect all NHX proteins to cause increased plant growth characteristics (e.g. yield enhancement or modified architecture) to monocotyledonous plants when grown under non-salt stress conditions. The specification does not teach which NHX protein would confer this trait and which would not. In the absence of guidance, undue experimentation would have been required by one skilled artisan at the time the claimed invention was made to isolate nucleic acid sequences encoding other NHX proteins from other sources and use them in improving plant growth characteristics under non-salt stress conditions. See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Claim 23 is directed to a homologue, derivative or an active fragment of a NHX protein including the one (SEQ ID NO: 2) encoded by SEQ ID NO: 1. Claim 32 is directed to a portion of SEQ ID NO: 1. A portion of SEQ ID NO: 1 would encompass a nucleic acid sequence encoding a fragment of SEQ ID NO: 2.

The instant specification fails to provide guidance on how to make nucleic acid sequences encoding a homologue of SEQ ID NO: 2 (NHX protein) having the functional

activity of improving plant growth characteristics.

The instant specification also fails to provide guidance on how to make nucleic acid sequences encoding a derivatives of SEQ ID NO: 2 (NHX protein) having the functional activity of improving plant growth characteristics.

The instant specification also fails to provide guidance on how to make nucleic acid sequences encoding a fragment or active fragments of SEQ ID NO: 2 (a NHX protein) having the functional activity of improving plant growth characteristics.

The specification, page 9, lines 31-37; page 11, lines 33-37 says:

> Homologues or derivatives of a protein encompass, peptides, oligopeptides, polypeptides, proteins having amino acid substitutions, deletions and/or insertions relative to the unmodified protein and having similar biological activity. Homologues or derivatives can also be produced by replacing amino acids having similar properties.

The specification, page 12, lines 31-37, says:

> An active fragment encompasses at least five contiguous amino acid residues of a NHX protein, or a C-terminal truncated version of a NHX protein, lacking one or more or all of the 100 amino acid residues of the NHX protein.

The specification does not provide guidance in the specification with respect to making amino acid changes (deletions, additions, substitutions and/or insertions) in a NHX protein, such as, the protein of SEQ ID NO: 2.

Thus, from the guidance in the specification, it would appear that the vast majority of the amino acids in a NHX protein of SEQ ID NO: 2 could be changed with any other amino acid.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO: 2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain Na^+/H^+ antiporter activity of the encoded protein. The

specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein.

Making amino acid changes in a NHX protein, such as, SEQ ID NO: 2 is unpredictable. While it is known that many amino acid substitutions, additions or deletions are generally possible in any given protein the positions within the protein's sequence where such amino acid changes can be made with a reasonable expectation of success (without altering protein function) are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see for example, Wells, Biochemistry 29:8509-8517, 1990, see pages 8511-8512, tables 1-2; Ngo et al., pp. 492-495,1994, see page 491, 1st paragraph).

Also see Guo et al. (PNAS, 101: 9205-9210, 2004, see page 9205, abstract; page 9206, table 1; page 9208, figure 1) who teach that there is a probability factor of 34% that a random amino acid replacement in a given protein will lead to its functional inactivation. In the instant case, such a probability factor will be much higher as the claim encompasses more than a single amino acid changes of the protein of NHX (SEQ ID NO: 2).

Also see, Keskin et al. (Protein Science, 13:1043-1055, 2004, see page 1043, abstract) who teach that proteins with similar structure may have different functions. Furthermore, Thornton et al. (Nature structural Biology, structural genomics

supplement, November 2000, page 992, 2nd paragraph bridging columns 1 and 2) teach that structural data may carry information about the biochemical function of the protein. Its biological role in the cell or organism is much more complex and actual experimentation is needed to elucidate actual biological function under *in vivo* conditions.

Thus, making and analyzing proteins with a large number of amino acid changes that also have NHX (Na+/H+ antiporter) activity of improving plant growth characteristics under non-salt stress conditions would require undue experimentation.

Claim 32 is directed to a nucleic acid sequence that would hybridize under any conditions of hybridization to the nucleotide sequence of SEQ ID NO: 1 or a portion thereof. The hybridization conditions described on page 13 of specification would encompass hybridization of nucleic acid sequences encoding a protein unrelated to instant SEQ ID NO: 2. This would also encompass hybridization of nucleic acid sequences that do not encode a protein.

It may be emphasized that it was very well established in the art (Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory (1982), see in particular, pages 387-389) at the time the claimed invention was made that in order to prevent hybridization of unrelated nucleic acid sequence(s) to a target sequence, hybridization and subsequent washing conditions must be highly stringent. For example, hybridization under conditions of 0.1-1.0x SSC, 50% formamide and 50 °C for 24 hours, followed by 2 washes in 0.1% SDS, 0.1x SSC at 65 °C for 25-30 minutes

each is considered highly stringent condition that would not allow hybridization of unrelated nucleic acid sequences to the target sequence.

Thus nucleic acid sequences that are unrelated in function to instant SEQ ID NO: 1 would be capable of hybridizing to SEQ ID NO: 1 under low stringent conditions of hybridization. This is because the breadth of the phrase "hybridizing" in claim 32 would encompass low stringent conditions of hybridization.

In the absence of adequate guidance, undue experimentation would have been required by a skilled artisan at the time the claimed invention was made to determine how to use nucleic acid sequences which would hybridize to SEQ ID NO: 1 or portions thereof under any condition of hybridization, in a method of improving growth characteristics in a monocotyledonous plant grown under non-salt stress conditions.

Additionally, the instant specification also fails to provide guidance on a method for improving monocotyledonous plant growth characteristics of improved yield and/or modified architecture comprising increasing expression of a nucleic acid encoding NHX protein (SEQ ID NO: 2) in any manner other than transforming a monocotyledonous plant with a nucleic acid sequence encoding SEQ ID NO: 2. The specification does not provide guidance on co-factors, or positive regulators of SEQ ID NO: 2, for example that makes the nucleic acid encoding NHX protein of SEQ ID NO: 2 to overexpress to produce a monocotyledonous plant with said characteristics. The specification provides no guidance on up-stream regulatory factors, for example, that may be necessary in stimulating the overexpression endogenous nucleic acid encoding NHX (SEQ ID NO: 2)

protein.

In the absence guidance, undue experimentation would have been required by a skilled artisan at the time the claimed invention was made to determine how a monocotyledonous plant with improved growth characteristics could have been produced by a method that comprises increasing the expression of a nucleic acid encoding NHX protein (SEQ ID NO: 2) in said plant without transforming the plant with a nucleic acid sequence encoding the protein of NHX (SEQ ID NO: 2). See Genentech, Inc. v. Novo Nordisk, A/S, USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

As the specification does not describe the transformation of a monocotyledonous plant with a nucleic acid sequence encoding any NHX protein, homologues, derivatives or fragments thereof, or sequences that hybridize to SEQ ID NO: 1, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with improved plant growth characteristic under non-salt stress conditions, if such plants are even obtainable.

Given the claim breadth, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

10. Claims 22-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to

comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Id.

See also MPEP Section 2163, page 174 of Chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function

and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Claims are broadly drawn to a method for improving plant growth characteristics, comprising increasing, in a monocotyledonous plant, expression of a nucleic acid encoding an NHX protein, wherein said plant is grown under non-salt stress condition, or wherein said nucleic acid encodes a homologue, derivative or active fragment of said NHX protein, or wherein said nucleic acid is a portion of SEQ ID NO: 1, or a sequence capable of hybridizing to SEQ ID NO: 1 or a portion thereof.

The essential feature of claim 22 is a nucleic acid sequence encoding any NHX protein.

The specification, describes a nucleic acid sequence (SEQ ID NO: 1) encoding rice Na^+/H^+ (NHX) antiporter protein of SEQ ID NO: 2. The specification also describes the function of NHX (SEQ ID NO: 2) in improving yield and/or modifying architecture of a monocotyledonous plant transformed with said nucleic acid, and grown under non-salt stress conditions. See pages 26-30, examples 1-3, table 3.

The specification does not describe the structure of the full scope of NHX proteins from diverse sources. The specification does not describe the function of NHX proteins from diverse sources. It may be emphasized that NHX is a member of complex Na^+/H^+ antiporter gene family, which have been implicated in diverse physiological processes. See for example, Brett et al. (Am. J. Physiol. Cell Physiol., 288:C223-C239, 2005; see page C223, 1st column, lines 5-12). Thus, Applicant's broadly claimed genus encompasses structures whose function is unrelated to the instantly claimed SEQ ID NO: 1 which encodes SEQ ID NO: 2. The specification does not describe the function of improving monocotyledonous plant growth characteristics (yield and/or architecture) for NHX proteins.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient elements of a NHX protein (SEQ ID NO: 2) encoded by SEQ ID NO: 1.

The only species described in the specification is SEQ ID NO: 1, which encodes SEQ ID NO: 2. Nucleic acid sequences encoding NHX proteins from diverse sources are not described, and thus their function of improving plant growth characteristics under non-salt stress conditions is not described.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 and its encoded protein of SEQ ID NO: 2 are insufficient to describe the claimed genus.

The essential feature of claim 23 is a nucleic acid encoding a homologue, derivative or active fragment of an NHX (encompasses SEQ ID NO: 2) protein. The essential feature of claim 32 is a portion of SEQ ID NO: 1. A portion of SEQ ID NO: 1 would encompass fragment(s) of SEQ ID NO: 1 encoding fragment(s) of SEQ ID NO: 2.

The specification, describes a nucleic acid (SEQ ID NO: 1) encoding rice Na+/H+ (NHX) antiporter protein of SEQ ID NO: 2. The specification also describes the function of SEQ ID NO: 2 in improving yield and/or modifying characteristics in a monocotyledonous plant transformed with said nucleic acid, and the plant is grown under non-salt stress conditions. See pages 26-30, examples 1-3, table 3.

The specification describes homologs or derivatives of NHX (SEQ ID NO: 2) as proteins having any % sequence identity to SEQ ID NO: 2, and comprising unspecified amino acid changes in the amino acid sequence of SEQ ID NO: 2 (page 9, lines 31-37; page 10, lines 9-11, page 12, lines 31-37).

The specification does not describe the structure of NHX homologues. The specification also does not describe the structure of SEQ ID NO: 2 homologues.

The specification does not describe the structure of any NHX derivatives, including derivatives of SEQ ID NO: 2.

The specification does not describe the structure of active fragments of NHX proteins.

The specification fails to describe the function of improving growth characteristics (yield and/or modified plant architecture) for said homologues, active fragments or derivatives of NHX proteins.

The specification also fails to describe the function of improving growth characteristics (yield and/or modified plant architecture) for functional fragments of SEQ ID NO: 2 or fragments encoded by a portion of SEQ ID NO: 1.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient elements of the NHX protein (SEQ ID NO: 2). It may be emphasized that NHX is a member of complex Na^+/H^+ antiporter gene family, which have been implicated in diverse physiological processes. See for example, Brett et al. (Am. J. Physiol. Cell Physiol., 288:C223-C239, 2005; see page C223, 1st column, lines 5-12). Thus, Applicant's broadly claimed genus encompasses structures whose function is unrelated to the NHX protein of SEQ ID NO: 2.

The only species described in the specification is SEQ ID NO: 1, which encodes SEQ ID NO: 2.

No homologs of SEQ ID NO: 2 are described in the specification and thus their function is unknown.

Nucleic acid sequences encoding NHX proteins from diverse sources are not described, and thus their function is unknown.

Nucleic acid sequences encoding active fragments of NHX proteins are not described and thus their function is unknown.

Since SEQ ID NO: 1 is described, and thus portions of SEQ ID NO: 1 are also described. However, function of said portions is not described.

Nucleic acid sequences encoding derivatives of SEQ ID NO: 2 (NHX protein) are not described and thus their function is unknown.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NOs: 1 and 2 are insufficient to describe the claimed genus.

The essential feature of the claim 32 is a sequence which is capable of hybridizing to SEQ ID NO: 1 or a portion thereof. The hybridization conditions described on page 13 of specification would encompass hybridization of nucleic acid sequences that are unrelated in function to SEQ ID NO: 1.

The specification does not describe the structure of nucleic acid sequences that would hybridize to SEQ ID NO: 1 under conditions (see page 13 of specification) which would allow hybridization of unrelated nucleic acid sequences to SEQ ID NO: 1. The specification does not describe structures of nucleic acid sequences which would hybridize to the nucleic acid sequence of SEQ ID NO: 1 or a portion thereof. The specification does not describe the function of improving growth characteristics (yield and/or modified plant architecture) for said hybridizing nucleic acid sequences when

expressed in a monocotyledonous plant, and the plant is grown under non-salt stress conditions.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient elements of a nucleic acid sequence of SEQ ID NO: 1.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 and its encoded protein (SEQ ID NO: 2) are insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described the following: (a) nucleic acids that encode NHX proteins from diverse sources, (b) nucleic acid sequences encoding homologs, derivatives or functional fragments of NHX proteins (c) function of a portion of SEQ ID NO: 1, and (d) nucleic acid sequences hybridizing to SEQ ID NO: 1 or a portion thereof, and the specification fails to provide an adequate written description of the claimed invention.

Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written Description guidelines published in Federal Register/Vol.66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide written description of the genus broadly claimed.

Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 22-25, and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukuda et al. (European Patent Publication No. EP 1143002, A1, Published October 10, 2001, Applicant's IDS).

Claims are drawn to a method for improving plant growth characteristics, comprising increasing, in a monocotyledonous plant, expression of a nucleic acid encoding an NHX protein, wherein said plant is grown under non-salt stress condition, or wherein said nucleic acid encodes a homologue, derivative or active fragment of said NHX protein, or wherein said nucleic acid is a portion of SEQ ID NO: 1, or a sequence capable of hybridizing to SEQ ID NO: 1, or a portion thereof, or wherein said growth characteristic is increased yield/biomass and/or modified plant architecture, or wherein said increased yield/biomass and/or modified plant architecture is increased

aboveground area, increased number of first panicles, increased plant height, increased total number of seeds, increased number of filled seeds, increased total seed weight, increased harvest index or increased thousand kernel weight, or wherein said nucleic acid is from a monocotyledonous plant of family Poaceae, or wherein said nucleic acid is from family Poaceae and genus *Oryza*, or plants having improved growth characteristics obtainable by said method.

Fukuda et al. disclose a method of making a transgenic rice plant comprising transforming a rice (monocotyledonous) plant with a nucleic acid sequence encoding a OsNHX1 protein of SEQ ID NO: 2, which has 100% sequence identity to instant SEQ ID NO: 2. The nucleic acid sequence (SEQ ID NO: 1) disclosed in the reference has also 100% sequence identity to instant SEQ ID NO: 1. The reference also discloses that the nucleic sequence used in making said transgenic plant is from rice, which is a monocotyledonous plant belonging to family Poaceae. The reference also discloses that the transformation comprises introducing and over-expressing the nucleic acid sequence encoding the OsNHX1 protein in said transgenic plant. The reference also discloses that the overexpression of the nucleic acid resulted in the increased expression of OsNHX1 protein in said rice plant. The reference also discloses that a nucleic acid sequence is capable of hybridizing to the nucleic acid sequence (SEQ ID NO: 1) encoding the OsNHX1 protein. The reference also discloses obtaining the transgenic rice plant from said method. See in particular, pages 7-8, example 1, paragraphs 0042-0044; pages 8-9, example 2-3, paragraphs 0046-0049; pages 21-22, claims 1-14, and 16; figures 1-3; SEQ ID NOs: 1 and 2.

It is important to note that the method of making transgenic plant disclosed in the reference uses a non-inducible and a constitutive promoter (CaMV 35S promoter, see paragraph 0049) in expressing the nucleic acid sequence encoding the OsNHX1protein. This implies that OsNHX1 would be expressed constitutively irrespective of the fact whether the plant is grown on salt-stress or non-salt stress conditions. The method of making a transgenic monocotyledonous plant of Fukuda et al. discloses all the active method steps that are required to practice the instantly claimed method. This also includes the method step of growing Fukuda et al. transgenic plant under non-salt stress conditions.

Although Fukuda et al. do not explicitly disclose increased yield/biomass and/or modified plant architecture consisting of increased aboveground area, increased number of first panicles, increased plant height, increased total number of seeds, increased number of filled seeds, increased total seed weight, increased harvest index or increased thousand kernel weight, such properties would be inherent to the method of over-expressing OsNHX1 protein (100% identity with instant SEQ ID NO: 2, which is encoded by SEQ ID NO: 1, emphasis added) in Fukuda et al. transgenic plant, unless the Applicant provides evidence to the contrary.

It is important to note that Fukuda et al. method of making monocotyledonous transgenic plant is identical to the instantly claimed method of making a monocotyledonous plant with improved characteristics. All the active method steps required to practice the instantly claimed method are disclosed by Fukuda et al.

See In re Cruciferous Sprout Litig., 301 F.3d 1343,1346-48, 64 USPQ2d 1202, 1204-05 (Fed. Cir. 2002) where a claim at issue was directed to a method of preparing a food rich in glucosinolates wherein cruciferous sprouts are harvested prior to the 2-leaf stage. The court held that the preamble phrase "rich in glucosinolates" helps define the claimed invention, as evidenced by the specification and prosecution history, and thus is a limitation of the claim (although the claim was anticipated by prior art that produced sprouts inherently "rich in glucosinolates").

Also, see *Integra LifeSciences I Ltd. V. Merck KGaA* 50 USPQ2d 1846, 1850 (DC Scalif 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then prior art anticipates the claimed invention.

Accordingly, Fukuda et al. anticipated the claimed invention.

12. Claims 22-25, and 30-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Fukuda et al. (US Patent No. 6,861,574 B2, Issued March 1, 2005, filed June 22, 2001).

Claims are drawn to a method for improving plant growth characteristics, comprising increasing, in a monocotyledonous plant, expression of a nucleic acid encoding an NHX protein, wherein said plant is grown under non-salt stress condition, or wherein said nucleic acid encodes a homologue, derivative or active fragment of said NHX protein, or wherein said nucleic acid is a portion of SEQ ID NO: 1, or a sequence capable of hybridizing to SEQ ID NO: 1, or a portion thereof, or wherein said growth characteristic is increased yield/biomass and/or modified plant architecture, or wherein

said increased yield/biomass and/or modified plant architecture is increased aboveground area, increased number of first panicles, increased plant height, increased total number of seeds, increased number of filled seeds, increased total seed weight, increased harvest index or increased thousand kernel weight, or wherein said nucleic acid is from a monocotyledonous plant of family Poaceae, or wherein said nucleic acid is from family Poaceae and genus *Oryza*, or plants having improved growth characteristics obtainable by said method.

Fukuda et al. disclose a method of making a transgenic rice plant comprising transforming a rice (monocotyledonous) plant with a nucleic acid sequence encoding a OsNHX1 protein of SEQ ID NO: 2, which has 100% sequence identity to instant SEQ ID NO: 2. The nucleic acid sequence (SEQ ID NO: 1) disclosed in the reference has also 100% sequence identity to instant SEQ ID NO: 1. The reference also discloses that the nucleic sequence used in making said transgenic plant is from rice, which is a monocotyledonous plant belonging to family Poaceae. The reference also discloses that the transformation comprises introducing and over-expressing the nucleic acid sequence encoding the OsNHX1 protein in said transgenic plant. The reference also discloses that the overexpression of the nucleic acid resulted in the increased expression of OsNHX1 protein in said rice plant. The reference also discloses that a nucleic acid sequence is capable of hybridizing to the nucleic acid sequence (SEQ ID NO: 1) encoding the OsNHX1 protein. The reference also discloses obtaining the transgenic rice plant from said method. See in particular, columns 10-11, example 1; columns 11-12, examples 2-3; claims 15-19; figures 1-3; SEQ ID NOs: 1 and 2.

It is important to note that the method of making transgenic plant disclosed in the reference uses a non-inducible and a constitutive promoter (CaMV 35S promoter, see column 12, example 2, line 47) in expressing the nucleic acid sequence encoding the OsNHX1 protein. This implies that OsNHX1 would be expressed constitutively irrespective of the fact whether the plant is grown on salt-stress or non-salt stress conditions. The method of making a transgenic monocotyledonous plant of Fukuda et al. discloses all the active method steps that are required to practice the instantly claimed method. This also includes the method step of growing Fukuda et al. transgenic plant under non-salt stress conditions.

Although Fukuda et al. do not explicitly disclose increased yield/biomass and/or modified plant architecture consisting of increased aboveground area, increased number of first panicles, increased plant height, increased total number of seeds, increased number of filled seeds, increased total seed weight, increased harvest index or increased thousand kernel weight, such properties would be inherent to the method of over-expressing OsNHX1 protein (100% identity with instant SEQ ID NO: 2, which is encoded by SEQ ID NO: 1, emphasis added) in Fukuda et al. transgenic plant, unless the Applicant provides evidence to the contrary.

It is important to note that Fukuda et al. method of making monocotyledonous transgenic plant is identical to the instantly claimed method of making a monocotyledonous plant with improved characteristics. All the active method steps required to practice the instantly claimed method are disclosed by Fukuda et al.

See In re Cruciferous Sprout Litig., 301 F.3d 1343,1346-48, 64 USPQ2d 1202, 1204-05 (Fed. Cir. 2002) where a claim at issue was directed to a method of preparing a food rich in glucosinolates wherein cruciferous sprouts are harvested prior to the 2-leaf stage. The court held that the preamble phrase "rich in glucosinolates" helps define the claimed invention, as evidenced by the specification and prosecution history, and thus is a limitation of the claim (although the claim was anticipated by prior art that produced sprouts inherently "rich in glucosinolates").

Also, see *Integra LifeSciences I Ltd. V. Merck KGaA* 50 USPQ2d 1846, 1850 (DC Scalif 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then prior art anticipates the claimed invention.

Accordingly, Fukuda et al. anticipated the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fukuda et al. (European Patent Publication No. EP 1143002, A1, Published October 10, 2001, Applicant's IDS), and further in view of Wu et al. (Plant cell Physiol. 39:885-889, 1998).

Claims are drawn to a method for improving plant growth characteristics, comprising increasing, in a monocotyledonous plant, expression of a nucleic acid encoding an NHX protein, wherein said plant is grown under non-salt stress condition, or wherein said nucleic acid is in sense orientation and is under the control of a tissue-specific promoter, a seed-specific promoter, an endosperm-specific promoter such as prolamin promoter.

Fukuda et al. teach a method of making a transgenic rice (monocotyledonous) plant comprising transforming a rice plant with a nucleic acid sequence encoding a OsNHX1 protein of SEQ ID NO: 2, which has 100% sequence identity to instant SEQ ID NO: 2. The nucleic acid sequence (SEQ ID NO: 1) taught in the reference has also 100% sequence identity to instant SEQ ID NO: 1. The reference also teaches that the nucleic sequence used in making said transgenic plant is from rice, which is a monocotyledonous plant belonging to family Poaceae. The reference also teaches that the transformation comprises introducing and over-expressing the nucleic acid

sequence encoding the OsNHX1 protein. The reference also teaches that the overexpression of the nucleic acid sequence resulted in the increased expression of OsNHX1 protein in said rice plant. See in particular, pages 7-8, example 1, paragraphs 0042-0044; pages 8-9, example 2-3, paragraphs 0046-0049; pages 21-22, claims 1-14, and 16; figures 1-3; SEQ ID NOs: 1 and 2. Fukuda et al. also teach that the nucleic acid sequence encoding the NHX (OsNHX1) protein was in sense orientation and operably linked to a CaMV 35S promoter. See page 9, paragraph 0049, line 4. Fukuda et al. also teach that rice is a monocotyledonous crop that has very low tolerance to salt, and is considered a salt sensitive plant species. See page 3, line 34. Fukuda et al. (2001) teachings are also discussed in previous rejection (see above).

Fukuda et al. do not teach a tissue-specific, seed-specific or an endosperm-specific promoter.

Wu et al. teach rice seed-specific promoter(s) that are active in transgenic seed-tissues. Wu et al. also teach an endosperm-specific prolamin promoter. See in particular, page 885, abstract; page 886, figure 1, table 1; page 887, figure 2.

At the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to modify the method of making a transgenic monocotyledonous plant (rice) as taught by Fukuda et al., to substitute the CaMV 35S promoter with a seed-specific or endosperm specific promoter of Wu et al., to obtain a transgenic rice plant and transgenic rice seeds derived thereof, expressing Fukuda et al. OsNHX1 protein from Wu et al. promoter.

It would have been obvious and within the scope of an ordinary skill in the art to use any seed-specific promoter including the seed-specific promoter(s) of Wu et al. in over-expressing Fukuda et al. OsNHX1 protein specifically in seed tissues.

Given that Fukuda et al. teach that rice is a naturally occurring salt-sensitive plant species, one of ordinary skill in the art would have been motivated to specifically overexpress Fukuda et al. OsNHX1 protein in the seeds so that the transgenic rice seeds thrive during germination when grown under naturally occurring salt concentrations with reasonable expectation of success. It may be emphasized that a naturally occurring soil in which most of the plant species grow normally would be considered a non-salt stress condition.

Thus, the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

15. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fukuda et al. (European Patent Publication No. EP 1143002, A1, Published October 10, 2001, Applicant's IDS), and in view of Chan et al. (Plant Molecular Biology, 22: 491-506, 1993).

Claims are drawn to a method for improving plant growth characteristics, comprising increasing, in a monocotyledonous plant, expression of a nucleic acid encoding an NHX protein, wherein said plant is grown under non-salt stress condition, or wherein said nucleic acid is in sense orientation and is under the control of weak constitutive promoter such as ubiquitin promoter minus first intron.

Fukuda et al. teachings are taught supra.

Fukuda et al. do not teach a weak constitutive promoter.

Chan et al. teach a method of making a transgenic rice (monocotyledonous plant) comprising constitutive expression of nptII coding sequence under the operable control of a weak promoter, such as, a nos promoter from *Agrobacterium*. Chan et al. also teach that the nos promoter exhibits uniform promoter activity in all tissues of a monocoyledonous plant (rice). See in particular, page 491, abstract; page 493, figure 1, materials and methods; page 494, paragraph bridging right and left columns; page 496.

At the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to modify the method of making a transgenic monocotyledonous plant (rice) as taught by Fukuda et al., to substitute the CaMV 35S promoter with any other constitutive promoter, including the nos promoter of Chan et al. to arrive at the instantly claimed invention with reasonable expectation of success.

Given that nos promoter exhibits uniform promoter activity in all tissues of a plant as asserted by Chan et al., one of the ordinary skill in the art would have been motivated to express Fukuda et al. NHX protein from Chan et al. promoter, for the purpose of obtaining a uniform (non-chimeric) plant phenotype (e.g. improved growth characteristics etc.) by uniform expression of Fukuda et al. NHX protein in all tissues of the transgenic plant.

It is important to note that Office contends that the recitation "such as" in claim 29 does not limit a weak constitutive promoter to maize ubiquitin promoter minus first intron. Thus claim 29 reads on any weak promoter including nopaline synthase (nos)

promoter of *Agrobacterium*. Also see page 17, lines 1-2 of the specification, wherein Applicant admits that nos promoter is considered to be a weak promoter.

Conclusions

16. Claims 22-33 are rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vinod Kumar 01-18-2008

Vinod Kumar
Patent Examiner
Art Unit 1638